IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	PEPYS
Serial No.	:	09/737,544
For	:	TREATMENT AND PREVENTION OF TISSUE DAMAGE
Filed	:	December 18, 2000
Examiner	:	Shengjun Wang
Art Unit	:	1617
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745 Fifth Avenue, New York, NY 10151

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SUBMISSION OF POWERPOINT PRESENTATION OF THOMAS J. KOWALSKI

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Dear Sir:

Submitted herewith is the PowerPoint presentation of Thomas J. Kowalski presented during the August 14, 2007 personal interview, for which the Examiner and his SPE are thanked for the courtesies extended. Applicant will be filing an Amendment, and also expects to file a Declaration, as discussed during the personal interview, likely by about September 4, 2007. From about September 15, 2007 onward Applicant's attorney looks forward to working with the Examiner to place the case in allowable condition prior to September 30, 2007, as also discussed during the interview.

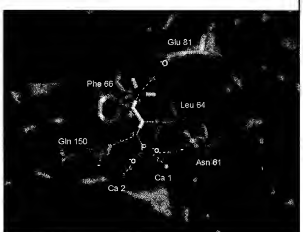
Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: /Thomas J. Kowalski/
Thomas J. Kowalski
Reg. No. 32,147
Angela M. Collison
Reg. No. 51,107
(212) 588-0800

- Case and statutory law
  - 35 USC 112: There is Enablement
    - Application teaches reducing tissue damage caused by CRP in a patient in need thereof who has suffered an inflammatory or tissue damaging condition, e.g., ischemic necrosis, stroke, comprising inhibiting CRP binding
    - Application teaches reducing damage to heart muscle caused by CRP in a patient who has suffered ischemic necrosis and is in need thereof by inhibiting CRP binding to its ligands *in vivo*
    - Presumption is that applicants have provided a patentable invention; burden is on USPTO to show by at least a preponderance that applicants are not entitled to a patent

- Case and statutory law
  - 35 USC 112: There is Enablement
    - Test is whether there is "undue experimentation" – *see, e.g.*, MPEP 2164.01
    - MPEP 2164.01(a) Undue Experimentation: "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff 'd. sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). *See also In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404."
    - "The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976)."

- Case and statutory law
  - 35 USC 112: There is Enablement



- Phosphocholine bound by CRP
- US Patent No. 4,640,913, "Phosphocholine Derivatives …"
- CRP binds to additional ligands, e.g., agar, barium sulfate, phosphorylated cellulose, sulfated polyacrylamide …
- NO UNDUE EXPERIMENTATION TO PRACTICE INVENTION

- Case and statutory law
  - 35 USC 102: An applicant shall be entitled to a patent …
    - Presumption is that applicants have provided a patentable invention; burden is on USPTO to show by at least a preponderance that applicants are not entitled to a patent
    - All evidence, the totality of the record, must be considered by PTO in asserting obviousness. *See In re Chu*, 36 USPQ2d 1089, 1095 (Fed. Cir. 1995); *see also In re Eli Lilly & Co.*, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990) (after rebuttal submitted, all evidence must be considered anew)

- Case and statutory law
  - *Rapoport v. Dement*, 59 USPQ2d 1215 (Fed. Cir. 2001):
    - **Preamble to be treated as a limitation, especially when used with post-transition reference thereto ("in need thereof")**
    - **Must look for the purpose a medicament was administered in the prior art to assert anticipation or obviousness: "There is no disclosure in the FPR Publication of tests in which buspirone is administered to patients suffering from sleep apnea with the intent to cure the underlying condition"**
  - Preamble in present claims must be considered as a limitation, and the intent or purpose for prior art must be considered

- Case and statutory law
  - No teaching or suggestion of reducing tissue damage caused by CRP in a patient in need thereof who has suffered an inflammatory or tissue damaging condition, e.g., ischemic necrosis, stroke, comprising inhibiting CRP binding to its ligands *in vivo or of* reducing damage to heart muscle caused by CRP in a patient who has suffered ischemic necrosis and is in need thereof by inhibiting CRP binding to its ligands *in vivo*

- Case and statutory law
  - *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970):
    - **"All words in a claim must be considered in judging patentability of that claim against the prior art"**
  - *Cont'l Can Co. v. Monsanto Co.,* 20 USPQ2d 1746, 1749 (Fed. Cir. 1991):
    - **"'inherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient'"**
  - All claim terms must be fully and fairly considered, and the claims cannot be said to be inherently anticipated or obvious

- Case and statutory law
  - *In re Shetty*, 195 USPQ 753, 756-57 (CCPA 1977):
    - "[T]he inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. **Obviousness cannot be predicated on what is unknown**"
  - *In re Naylor,* 152 USPQ 106, 108 (CCPA 1966):
    - "**[Inherency] is quite immaterial if … one of ordinary skill in the art would not appreciate or recognize the inherent result**"
  - *In re Marshall*, 198 USPQ 344 (CCPA 1978):
    - "An accidental or unwitting duplication of an invention cannot constitute anticipation …"
  - **Thus, the present invention was not anticipated and is nonobvious – It was unknown in the art!**

- Case and statutory law
  - *In re Fine,* 5 USPQ 2d 1596, 1599 (Fed. Cir. 1988):
    - "Obvious to try" is not the standard under 35 USC §103
    - *In re Fritch,* 23 USPQ 2d 1788, 1783-1784 (Fed. Cir. 1992) ("The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious"); *see also In re Laskowski*, 10 USPQ2d 1397, 1399 (Fed. Cir. 1989); *In re Geiger*, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987)
  - *In re Dow*, 5 USPQ2d 1531-1532 (Fed. Cir. 1988):
    - "[t]here must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure"
  - *KSR* inapplicable as it dealt with assembly of old elements; "obvious to try" still not a standard under KSR; and the result of the instant invention is not an expected result (from an assembly of old elements as in *KSR*)

- Case and statutory law
  - In sum, under the law, there must be some teachings, suggestion or expectation in the art of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - It was NOT taught, suggested, or expected that one would want to INHIBIT CRP binding to its ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - In contrast to the art – especially the art of record – the instant invention involves inhibiting binding of CRP to its ligands *in vivo* to reduce tissue damage – to reduce stroke, ischemic necrosis
  - The instant invention is not expected from the prior art; not taught or suggested by the prior art

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar ; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - Rather, there is a disclosure of various vast genuses, e.g.,
    - PLA2 inhibitors can be classified into numerous types:
      - I. Phosphatidylethanolamine
      - II. N-methyl-PE derivatives and their analogues, linked through the amino group of the N-methyl-PE by a covalent bond
      - III. N,N-dimethyl-PE derivatives and their analogues linked through the amino group of the N,N-dimethyl-PE by a covalent bond.

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar ; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - Rather, there is a disclosure of various vast genuses, e.g.,
    - PLA2 inhibitors can be classified into numerous types:
      - IV. Phosphatidylserine (PS) and its analogues, such as palmitoyl-stearoyl-PS (which gave the best results). Natural PSs from various sources, semisynthetic PSs, synthetic natural and artifactual PSs and their isomers
      - V. Glycerol ether, amine, amide, thioether, ester and thioester
      - VI. Ethylene glycol derivatives of the general formula
      - VII. Aminopiperazine and its derivatives

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - Rather, there is a disclosure of various vast genuses, e.g.,
    - PLA2 inhibitors can be classified into numerous types:
      - VIII. Manoalide and its derivatives, synthetic and natural, e.g., manoalogue
      - IX. Arachidonic acid and its derivatives, natural and synthetic
      - X. p-methoxyphentylamine, its analogues and derivatives
      - XI. Sphingosines, their analogues and derivatives
      - XII. Phenacylbromides

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar ; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - Rather, there is a disclosure of various vast genuses, e.g.,
    - PLA2 inhibitors can be classified into numerous types:
      - Glycerol ether, amine, amide, thioether, ester and thioester derivatives of the general formula …
      - phosphoryl-serine, phosphorylethanolamine, phosphoryl-glycerol, phosphoryl inositol, etc., linked to the carrier moiety via the R; and where X is -O-, -S-
      - NH-can be linked to carriers … ethylene glycol monoether phosphatidyl compounds

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar ; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - Rather, there is a disclosure of various vast genuses, e.g.,
    - PLA2 inhibitors can be classified into numerous types:
      - Derivatives of p-methoxyphenetylamine that can be bound to a carrier molecule, e.g., dextramine
      - preferred inhibitors being phosphatidylserine linked directly to or via a divalent bridging moiety to a carrier

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar ; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - Rather, there is a disclosure of various vast genuses, e.g.,
    - PLA2 inhibitors can be classified into numerous types:
      - activity of PLA2 in cell surface membranes with cellular secretion in general
      - Regulation of PLA2 in cell surface membranes … a treatment for pathological conditions associated with oversecretion of these substances, such as occurs in allergic response, inflammation, thrombosis, hypertension, and neurological disorders, among others

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar ; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - Rather, there is a disclosure of various vast genuses, e.g.,
    - PLA2 inhibitors can be classified into numerous types:
      - animals, including but not limited to mammals, e.g., livestock, households pets, humans, cattle, cats, dogs, poultry, etc.

- Prior art does not teach or suggest the invention
  - No mention or suggestion in Yedgar of administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
  - Yedgar cannot be cited for anticipation; claimed invention is not readily envisioned from Yedgar ; *cf.* MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus)
  - And compounds therein cannot function as recited in instant claims:
    - The primary role of the carrier moiety is to increase the size (molecular volume) of the PLA2 inhibitor forming the PLA2-inhibitor moiety of the composition of this invention sufficient to render the latter cell impermeable
    - The carriers can have a wide range of molecular weight, e.g., above 50,000 (up to a few hundred thousands)

- Prior art does not teach or suggest the invention
  - Bhakdi only pertains to binding of CRP to ENHANCE Complement Activity, but does not teach or suggest that binding of CRP and enhancing complement activity are NOT desirable or that one would want to INHIBIT binding of CRP and Complement Activity
  - Yedgar, Kitao and Wissner does NOT remedy deficiencies of Bhakdi
    - They do not teach or suggest administering compound that binds to CRP to inhibit its binding to ligands *in vivo* to reduce tissue damage – stroke, ischemic necrosis
      - Yedgar addressed above; does NOT address CRP inhibiting binding of CRP and Complement Activity to reduce tissue damage
      - Kitao involves binding of CRP with lipoproteins using gel filtration and macrophage ingestion
      - Wissner only addresses Phosphocholine derivatives as antihypertensives
  - Presently claimed invention is patentable over art of record!